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Reference: [Docket Number 03D-0060] "FDA Draft Guidance for Industry – 21 CFR Part 11; Scope and Application"

To Whom It May Concern,

Merck KGaA (not linked to Merck & Co) appreciates FDA's effort to provide guidance on 21 CFR Part 11 and the opportunity to provide comments on this new guidance document.

Please find enclosed our comments on the Draft Guidance for Industry – 21 CFR Part 11; Electronic records; Electronic signatures; Scope and Application, Docket Number 03D-0060.

For questions please refer to:

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Sincerely,

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03D-0060

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In general, we appreciate FDA's approach to narrowly interpret Part 11 especially with regard to generated paper print-outs meeting all predicate rule requirements and being relied upon to perform regulated activities not triggering Part 11. The ability to retain electronic record information in ways other than electronic form to meet long-term retention periods will be particularly useful.

Overall the guideline helps to clarify many previous issues but raises further questions.

Additional clarification on the Part 11 status of configuration data of computerized systems as well as on the status of small devices (e.g. programmable logic controllers = PLC) that are widely used in modern manufacturing sites would be highly appreciated.

I. Introduction

Line 43: [...] (commonly known as existing or legacy systems) [...]

Comment: It is our understanding that legacy systems are systems that were set operative prior to August 20 1997. The term 'existing systems' would cover both systems that are legacy systems (as previously defined) and systems that were set operative between August 20 1997 and now.

Suggested change: Delete the underlined words.

III. A. Overall Approach to Part 11 Requirements

Lines 120 - 123: For those records that we are now clarifying are subject to Part 11, we intend to exercise enforcement discretion with regard to Part 11 requirements for validation, audit trails, record retention, and record copying, in the manner described in this guidance, and in applying Part 11 to systems that were operational before the effective date of Part 11.

Comment: It is not clear whether the intention is that the discretion is to be executed by investigators based on their best knowledge on a system-by-system basis, or if the intention is that execution will be based on criteria defined in Agency guidelines.

Suggested change: We suggest clarifications be added in the final guidance as we feel it is essential for a clear understanding of Part 11 requirements on validation, audit trail, legacy system, copies of electronic records and record retention.

Lines 128 – 132: [...](e.g., limiting system access to authorized individuals; use of operational system checks; use of authority checks; use of device checks; determination that persons who develop, maintain, or use electronic systems have the education, training, and experience to perform their assigned tasks; establishment of and adher-

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ence to written policies that hold individuals accountable for actions initiated under their electronic signatures; and appropriate controls over systems documentation) [...]

Comment: It would be helpful if the items listed in parentheses were directly related to the rule elements they reflect.

III. B. 2 Definition of Electronic records

Lines 172 - 176: [...] For example, if a record is required to be maintained by a predicate rule and you use a computer to generate a paper printout of the electronic records, but you nonetheless rely on the electronic record to perform regulated activities, the Agency may consider you to be *using* the electronic record instead of the paper record. [...]

Comment: This may open an area of debate since the term "rely on the electronic record" allows interpretation; e.g. if one prints out an analytical record, which contains calculated results from a computerized system, and the quality decision is based on that print-out, one may conclude that Part 11 is not triggered.

Suggested change: Clarify the underlined term.

Lines 191, 192: [...] Electronic signatures that are intended to be the equivalent of handwritten signatures, initials, and other general signings required by predicate rules

Comment: Electronic signatures are legally binding equivalents of handwritten signatures. To prevent any misunderstanding we recommend avoiding terms like initials and/or general signings in this context.

Suggested change: Delete the underlined words.

III. C. 1 Validation

Lines 212 - 214: For further guidance on validation of computerized systems, see FDA's guidance for industry and FDA Staff *General Principles of Software Validation* and also industry guidance such as the *GAMP 4 Guide* (See References).

Comment: We welcome FDA's acknowledgement of sound industry standards. However, referencing only one industry standard on validation of computerized systems without mentioning the other standards will open an area of debate on the appropriateness of other existing industry standards on the validation of computerized systems. Additionally, the referenced FDA guidance *General Principles of Software Validation* applies to the validation of medical device software or the validation of software used to design, develop, or manufacture medical devices.

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Suggested change: Delete the underlined term. Add the area of application for the FDA guidance *General Principles of Software Validation* that is applicable to the validation of medical device software or the validation of software used to design, develop, or manufacture medical devices.

III. C. 3 Legacy Systems

Lines 236, 237: The Agency intends to exercise enforcement discretion with regard to legacy systems that otherwise met predicate rule requirements prior to August 20, 1997, the effective date of Part 11. [...]

Comment: Today, many legacy systems that were set operative prior to August 20, 1997 have been partly changed in the meantime. The guideline does not state what kind of changes would trigger Part 11.

Suggested change: A computerized system that was set in operation prior to August 20, 1997 is a legacy system if the system has not been subject to changes in the meantime which impact the creation, modification, maintenance, archiving, retrieval or transmission of electronic records.

III. C. 4 Copies of Records

Lines 258, 259: [...] If you have the ability to search, sort, or trend Part 11 records, copies provided to the Agency should provide the same capability if it is technically feasible. [...]

Comment: The described functionalities are substantial new requirements that are not covered by the original rule as the requirements for electronic records are defined according to 11.10 (b) as "the ability to generate accurate and complete [electronic] copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency." It is our understanding that this does not imply search, sort or trend capabilities for electronic copies of electronic records. Also the term used "if technically feasible" may open a large area of debate.

Suggested change: Delete the underlined sentence.

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III. C. 5 Record Retention

Lines 275 – 277: FDA normally does not intend to object if you decide to archive required records in electronic format to nonelectronic media such as microfilm, microfiche, and paper, or to a standard electronic file format, such as PDF.

Comment: The possibility to migrate electronically archived data to ensure further accessibility of the data is not reflected in the guideline.

Suggested change: Include a statement on record migration.

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